WHAT IS CLAIMED IS:

1. An oligopeptide that comprises a sequence of amino acids that is recognized and selectively proteolytically cleaved by free prostate specific antigen.

2. The oligopeptide according to Claim 1 wherein the sequence of amino acids is

a) AsnLysIleSerTyrGln|Ser (SEQ.ID.NO.: 13),

b) LysIleSerTyrGln|Ser (SEQ.ID.NO.: 14),

c) GlyGluAsnGlyValGlnLysAspValSerGlnXaaSerIleTyr|SerGlnThrGlu (SEQ.ID.NO.: 15) ,

d) GlyLysGlyIleSerSerGlnTyr|SerAsnThrGluGluArgLeu (SEQ.ID.NO.: 2),

e) AsnLysIleSerTyrTyr|Ser (SEQ.ID.NO.: 127),

f) AsnLysAlaSerTyrGln|Ser (SEQ.ID.NO.: 128),

g) SerTyrGln|SerSer (SEQ.ID.NO.: 129);

h) LysTyrGln|SerSer (SEQ.ID.NO.: 140); or

i) hArgTyrGln|SerSer (SEQ.ID.NO.: 141);

wherein hArg is homoarginine and Xaa is any natural amino acid.

3. The oligopeptide according to Claim 2 wherein the sequence of amino acids is

129

a) AsnLysIleSerTyrGln|SerSer (SEQ.ID.NO.: 16),

b) AsnLysIleSerTyrGln|SerAla (SEQ.ID.NO.: 130),

c) AsnLysIleSerTyrGln|SerSerSer (SEQ.ID.NO.: 17),

d) AlaAsnLysIleSerTyrGln|SerSerSer (SEQ.ID.NO.: 18),

e) LysIleSerTyrGln|SerSerSerThrGlu (SEQ.ID.NO.: 19),

f) GlyGluAsnGlyValGlnLysAspValSerGlnArgSerIleTyr|SerGlnThrGlu (SEQ.ID.NO.: 4),

g) GlyGluAsnGlyValGlnLysAspValSerGlnSerSerIleTyr|SerGlnThrGlu (SEQ.ID.NO.: 5),

h) AlaAsnLysIleSerTyrTyr|Ser (SEQ.ID.NO.: 131),

i) AlaAsnLysAlaSerTyrGln|Ser (SEQ.ID.NO.: 132),

j) SerTyrGln|SerSerThr (SEQ.ID.NO.: 133),

k) SerTyrGln|SerSerSer (SEQ.ID.NO.: 134),

l) LysTyrGln|SerSerSer (SEQ.ID.NO.: 142),

m) hArgTyrGln|SerSerSer (SEQ.ID.NO.: 143), or

n) SerTyrGln|SerSerLeu (SEQ.ID.NO.: 135).

4. The oligopeptide according to Claim 2 wherein the amino acid sequence is

a) AsnLysIleSerTyrGln |SerSerSerThr (SEQ.ID.NO.: 10),

b) AlaAsnLysIleSerTyrGln|SerAla (SEQ.ID.NO.: 136),

c) AsnLysIleSerTyrGln|SerSerSerThrGlu (SEQ.ID.NO.:3),

d) AlaAsnLysIleSerTyrGln|SerSerSerThrGlu (SEQ.ID.NO.: 11),

e) GlyGluAsnGlyValGlnLysAspValSerGlnArgSerIleTyr|SerGlnThrGlu (SEQ.ID.NO.: 4),

f) AlaAsnLysIleSerTyrTyr|SerSer (SEQ.ID.NO.: 137),

g) AlaAsnLysIleSerTyrTyr|SerAla (SEQ.ID.NO.: 138),

h) AlaAsnLysAlaSerTyrGln|SerAla (SEQ.ID.NO.: 139), or

i) AlaSerTyrGln|SerSerLeu (SEQ.ID.NO.: 94).

5. The oligopeptide according to Claim 2 wherein the amino acid sequence is

a) GlyArgLysAlaAsnLysIleSerTyrGln|SerSerSerThrGluGluArgArg LeuHisTyr GlyGluAsnGly (SEQ.ID.NO.: 6).

6. The oligopeptide according to Claim 1 which is selected from:

AsnArgIleSerTyrGln|Ser (SEQ.ID.NO.: 21),
AsnLysValSerTyrGln|Ser (SEQ.ID.NO.: 22),
AsnLysMetSerTyrGln|SerSer (SEQ.ID.NO.: 23),
AsnLysLeuSerTyrGln|SerSer (SEQ.ID.NO.: 24),
AsnLysIleThrTyrGln|SerSerSer (SEQ.ID.NO.: 25),

AsnLysIleSerPheGln|SerSerSer (SEQ.ID.NO.: 26),
AsnLysIleSerTrpGln|SerSerSerThr (SEQ.ID.NO.: 27),
AsnLysIleSerTyrAsn|SerSerSerThr (SEQ.ID.NO.: 28),
AsnLysIleSerTyrGln|ThrSerSerThr (SEQ.ID.NO.: 29),
AsnLysIleSerTyrGln|Ser (SEQ.ID.NO.: 30),
GlnLysIleSerTyrGln|SerSer (SEQ.ID.NO.: 31),
AsnArgIleThrTyrGln|SerSerSer (SEQ.ID.NO.: 32),
AsnArgIleSerPheGln|SerSerSerThr (SEQ.ID.NO.: 33),
AsnArgIleSerTrpGln|SerSerSerThr (SEQ.ID.NO.: 35),
AsnArgIleSerTyrGln|ThrSerSerThr (SEQ.ID.NO.: 36),
AsnLysIleThrTyrGln|ThrSerSerThr (SEQ.ID.NO.: 37),
AsnLysLeuSerTyrGln|ThrSerSerThr (SEQ.ID.NO.: 38),
GlnLysLeuSerTyrGln|SerSerSerThr (SEQ.ID.NO.: 39),
AsnArgLeuSerTyrGln|ThrSerSerThr (SEQ.ID.NO.: 40),
AsnLysValSerPheGln|SerSerSerThr (SEQ.ID.NO.: 41),
AsnArgValSerTrpGln|SerSerSerThr (SEQ.ID.NO.: 42),
GlnLysValSerTyrGln|SerSerSerThr (SEQ.ID.NO.: 43),
GlnLysIleSerTyrGln|ThrSerSerThr (SEQ.ID.NO.: 34), or
AsnLysIleSerTyrGln|SerSerSerThr (SEQ.ID.NO.: 44).

7. The oligopeptide according to Claim 1 which is

AlaAsnLysIleSerTyrGln|SerSerSerThrGlu-amide (SEQ.ID.NO.: 11)
Ac-AlaAsnLysIleSerTyrGln|SerSerSerThrLeu (SEQ.ID.NO.: 70)

Ac-AlaAsnLysIleSerTyrGln|SerSerSerThrGlu-amide (SEQ.ID.NO.: 11)
Ac-AlaAsnLysIleSerTyrGln|SerSerSerThrLeu-amide (SEQ.ID.NO.: 70)
Ac-AlaAsnLysIleSerTyrGln|SerAlaSerThrGlu-amide (SEQ.ID.NO.: 73)
Ac-AlaAsnLysIleSerTyrGln|SerSerLysThrGlu-amide (SEQ.ID.NO.: 74)
Ac-AlaAsnLysIleSerTyrGln|SerSerThrGlu-amide (SEQ.ID.NO.: 75)
Ac-AlaAsnLysIleSerTyrGln|SerSerGlnThrGlu-amide (SEQ.ID.NO.: 78)
Ac-AlaAsnLysIleSerTyrGln|SerAlaLysThrGlu-amide (SEQ.ID.NO.:79)
Ac-AlaAsnLysIleSerTyrGln|SerThrGlu-amide (SEQ.ID.NO.: 81)
Ac-AlaAsnLysSerTyrGln|SerSerThrGlu-amide (SEQ.ID.NO.: 82)

103

Ac-AlaAsnLysAlaSerTyrGln|SerAlaSerThrGlu-amide (SEQ.ID.NO.: 84)
Ac-AlaAsnGluIleSerTyrGln|SerAlaSerThrGlu-amide (SEQ.ID.NO.: 85)
Ac-AsnLysIleSerTyrGln|SerSer-amide (SEQ.ID.NO.: 16)
Ac-LysIleSerTyrGln|SerSer-amide (SEQ.ID.NO.: 86)
Ac-SerTyrGln|SerSerThrGlu-amide (SEQ.ID.NO.: 87)
Ac-AlaSerTyrGln|SerSerThrGlu-amide (SEQ.ID.NO.: 89)
Ac-AlaAsnLysIleSerTyrTyr|SerSerSerThrGlu-amide (SEQ.ID.NO.: 92)
Ac-AlaAsnLysIleSerTyrTyr|SerAlaSerThrGlu-amide (SEQ.ID.NO.: 93)
Ac-AlaSerTyrGln|SerSerLeu-amide (SEQ.ID.NO.: 94)
Ac-AlaAsnSerTyrGln|SerSerSerThrGlu-amide (SEQ.ID.NO.: 95)
Ac-AlaSerTyrGln|SerSerSerThrGlu-amide (SEQ.ID.NO.: 96)
Ac-SerTyrGln|SerSerSerThrGlu-amide (SEQ.ID.NO.: 97) or
Ac-AlaAsnLysAlaSerTyrGln|SerAlaSerCys-amide (SEQ.ID.NO.: 98).

8. An assay for determining proteolytic activity of free prostate specific antigen in a sample, comprising the steps of:

(a), reacting a substrate, wherein the substrate is an oligopeptide that comprises a sequence of amino acids that is recognized and selectively proteolytically cleaved by free prostate specific antigen, with the sample; and

(b), detecting whether the substrate has been cleaved.

9. The assay according to Claim 8 wherein the step of detecting whether the substrate has been cleaved comprises analyzing the assay mixture by high performance liquid chromatography.

10. An assay for identifying compounds which inhibit the proteolytic activity of prostate specific antigen, comprising:

(a), reacting a substrate, wherein the substrate comprises a sequence of amino acids that is recognized and selectively proteolytically cleaved by free prostate specific antigen, with free prostate

specific antigen in the presence of a test substance; and

(b), detecting whether the substrate has been cleaved, in which the ability of the test substance to inhibit proteolytic activity of prostate specific antigen is indicated by a decrease in the cleavage of the substrate as compared to the cleavage of the substrate in the absence of the test substance.

11. The assay according to Claim 10 wherein the step of detecting whether the substrate has been cleaved comprises analyzing the assay mixture by high performance liquid chromatography.

~~12. A conjugate which is useful for the treatment of prostate cancer which comprises a cytotoxic agent attached to a oligopeptide, wherein the oligopeptide comprises a sequence of amino acids that is recognized and selectively proteolytically cleaved by free prostate specific antigen, wherein the means of attachment is a covalent bond or a chemical linker.~~

~~13.~~ The conjugate according to Claim ~~12~~ wherein the cytotoxic agent is a member of a class of cytotoxic agents selected from the following classes:

a) anthracycline family of drugs,
b) the vinca alkaloid drugs,
c) the mitomycins,
d) the bleomycins,
e) the cytotoxic nucleosides,
f) the pteridine family of drugs,
g) diynenes,
h) estramustine,
i) cyclophosphamide, and
h) the podophyllotoxins.

B

3 ~~14.~~ The conjugate according to Claim ~~12~~ 21 wherein the cytotoxic agent is selected from the following cytotoxic agents:

a) doxorubicin,
b) carminomycin,
c) daunorubicin,
d) aminopterin,
e) methotrexate,
f) methopterin,
g) dichloro-methotrexate,
h) mitomycin C,
i) porfiromycin,
j) 5-fluorouracil,
k) 6-mercaptopurine,
l) cytosine arabinoside,
m) podophyllotoxin,
n) etoposide,
o) etoposide phosphate,
p) melphalan,
q) vinblastine,
r) vincristine,
s) leurosidine,
t) vindesine,
u) estramustine,
v) cisplatin,
w) cyclophosphamide, and
x) leurosine.

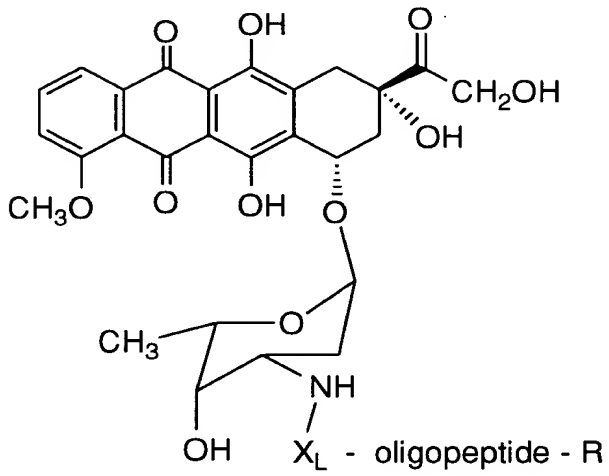
B

4 ~~15.~~ The conjugate according to Claim ~~12~~ 21 wherein the cytotoxic agent is selected from doxorubicin and vinblastine or a cytotoxic derivative thereof.

B

5 ~~16.~~ The conjugate according to Claim ~~12~~ 21 wherein the cytotoxic agent is doxorubicin or a cytotoxic derivative thereof.

17. The conjugate according to Claim 16 of the formula I:



I

wherein:

oligopeptide is an oligopeptide which is specifically recognized by the free prostate specific antigen (PSA) and is capable of being proteolytically cleaved by the enzymatic activity of the free prostate specific antigen;

X_L is absent or is an amino acid selected from:

a) phenylalanine,
b) leucine,
c) valine,
d) isoleucine,
e) (2-naphthyl)alanine,
f) cyclohexylalanine,
g) diphenylalanine,
h) norvaline, and
j) norleucine;

R is hydrogen or $-(C=O)R^1$; and

R^1 is C_1-C_6-alkyl or aryl.

~~18~~ 16. The conjugate according to Claim ~~17~~ wherein:

oligopeptide is an oligomer that comprises an amino acid sequence selected from:

a) AsnLysIleSerTyrGln|Ser (SEQ.ID.NO.: 13),

b) LysIleSerTyrGln|Ser (SEQ.ID.NO.: 14),

c) GlyGluAsnGlyValGlnLysAspValSerGlnXaaSerIleTyr|SerGlnThrGlu (SEQ.ID.NO.: 15) ,

d) GlyLysGlyIleSerSerGlnTyr|SerAsnThrGluGluArgLeu (SEQ.ID.NO.: 2),

e) AsnLysIleSerTyrTyr|Ser (SEQ.ID.NO.: 127),

f) AsnLysAlaSerTyrGln|Ser (SEQ.ID.NO.: 128),

g) SerTyrGln|SerSer (SEQ.ID.NO.: 129), and

h) hArgTyrGln|SerSer (SEQ.ID.NO.: 141);

wherein hArg is homoarginine and Xaa is any natural amino acid;

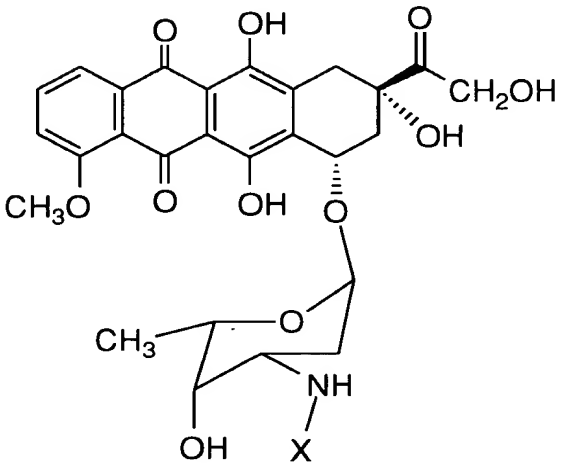
X_L is absent or is an amino acid selected from:

a)leucine,
b) isoleucine, and
d) valine; and

R is acetyl, pivaloyl or benzoyl.

133

8~~9~~. The conjugate according to Claim ~~16~~ 15 which is selected from:



wherein X is:

H_2N— AsnLysIleSerTyrGlnSer—C(=O)— (SEQ.ID.NO.: 13),

H_2N— AsnLysIleSerTyrGlnSerSer—C(=O)— (SEQ.ID.NO.: 16),

H_2N— AsnLysIleSerTyrGlnSerSerSer—C(=O)— (SEQ.ID.NO.: 17),

H_2N— AsnLysIleSerTyrGlnSerSerSerThr—C(=O)— (SEQ.ID.NO.:10),

H_2N—AsnLysIleSerTyrGlnSerSerSerThrGlu—C(=O)— (SEQ.ID.NO.: 3),

H_2N— AlaAsnLysIleSerTyrGlnSerSerSerThrGlu—C(=O)— (SEQ.ID.NO.: 11),

AcHN—AlaAsnLysIleSerTyrGlnSerSerSerThr—C(=O)— (SEQ.ID.NO.: 117),

AcHN—AlaAsnLysIleSerTyrGlnSerSerSerThrLeu—C(=O)— (SEQ.ID.NO.: 70),

AcHN—AlaAsnLysAlaSerTyrGlnSerAlaSerThrLeu—C(=O)— (SEQ.ID.NO.: 118),

AcHN—AlaAsnLysAlaSerTyrGlnSerAlaSerLeu—C(=O)— (SEQ.ID.NO.: 119),

AcHN—AlaAsnLysAlaSerTyrGlnSerSerSerLeu—C(=O)— (SEQ.ID.NO.: 120),

AcHN—AlaAsnLysAlaSerTyrGlnSerSerLeu—C(=O)— (SEQ.ID.NO.: 121),

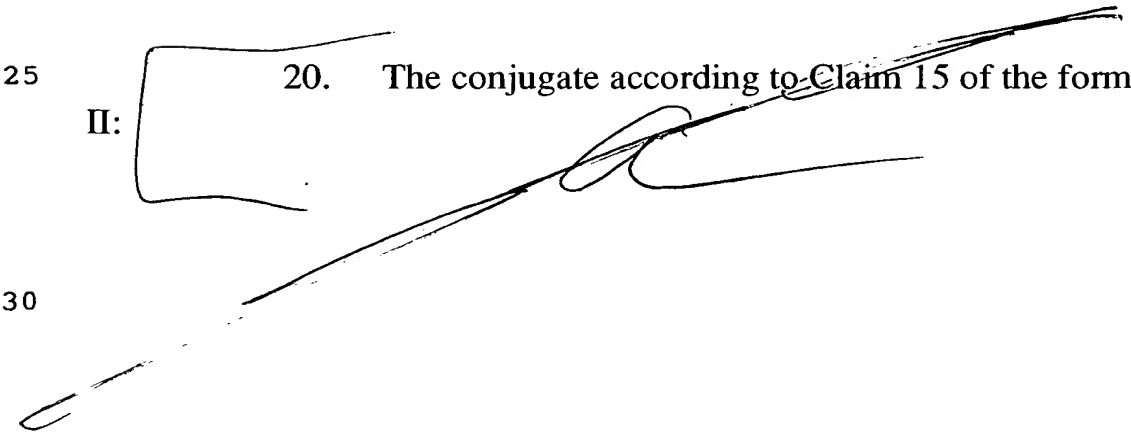
AcHN—SerTyrGlnSerSerSerLeu—C(=O)— (SEQ.ID.NO.: 144),

AcHN—hArgTyrGlnSerSerSerLeu—C(=O)— (SEQ.ID.NO.: 145),

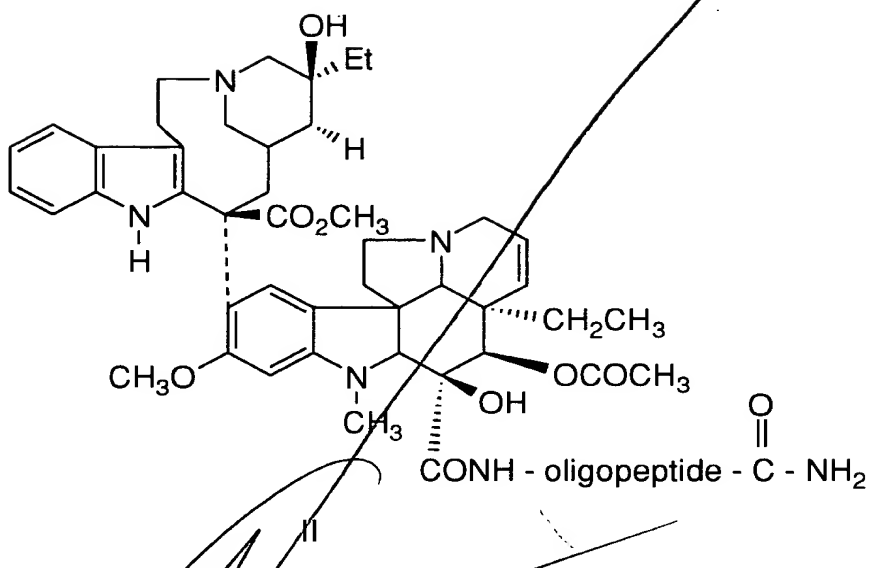
AcHN—LysTyrGlnSerSerSerLeu—C(=O)— (SEQ.ID.NO.: 124), or

AcHN—LysTyrGlnSerSerNle—C(=O)— (SEQ.ID.NO.: 146).

20. The conjugate according to Claim 15 of the formula II:



135



wherein:

oligopeptide is an oligopeptide which is specifically recognized by the free prostate specific antigen (PSA) and is capable of being proteolytically cleaved by the enzymatic activity of the free prostate specific antigen.

add B'7

136